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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/554,191	08/03/2006	Darrell H. Reneker	089498.0449.US	2634

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EXAMINER	
BUCKLEY, AUDREA	

ART UNIT	PAPER NUMBER
1617	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/554,191	RENEKER ET AL.	
	Examiner	Art Unit	
	AUDREA J. BUCKLEY	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 December 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,5-15,17-25,35,36 and 39-48* is/are pending in the application.

4a) Of the above claim(s) *15 and 17-25* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,5-14,35,36 and 39-48* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/6/2010*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

Applicants' remarks and amendments filed 12/06/2010 have been entered. Claims 3, 4, 16, 37, and 38 were canceled; claims 26 through 34 previously were canceled. Claims 15 and 17-25 are withdrawn. Claims 1, 2, 35, 36, and 46 stand amended. No new claims were added.

Applicant's election without traverse in the reply filed on 4/16/2010 is acknowledged. The election requirement between Groups I and II is deemed proper and is maintained and therefore made FINAL.

Accordingly, claims 1, 2, 5-14, 35, 36, and 39-48 are under current examination.

Priority

This application is a 371 of PCT/US04/12673, filed 04/23/2004, which claims benefit of 60/464, 879, filed 4/23/2003.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on 12/06/2010 is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement has been considered by the examiner.

Withdrawn Claim Rejections

All rejections not re-iterated herein are withdrawn in light of Applicants' amendments to the claims filed 12/06/2010.

New Grounds of Rejection

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 2, 5-7, 9-11, 13, 14, 35, 36, 39-41, 44, 45, 47, and 48 are rejected under 35 U.S.C. 103(a) as being unpatentable over Seitz, *et al.* (WO 01/89572 A1, published November 29, 2001, newly cited, submitted in IDS dated 1/10/2006) in view of Wheatley, *et al.* (WO 02/00149 A1, published January 3, 2002, newly cited, submitted in IDS dated 1/10/2006).

Regarding claims 1, 6, 7, 10, 11, 14, 35, 40, 41, 44, 45, and 48, the Seitz reference teaches a biocompatible system for generating nitric oxide from sodium nitrite, ascorbic acid, and maleic acid upon treatment with water (see page 4, lines 9-14, 18, and 26-28). The reactants can be sequestered in separate gels that are then admixed or applied as layers to a substrate such as skin. The reactants are released from gels and are thereby allowed to react to form NO. The reaction rate can be controlled by adjusting the rate of release from the gel. See e.g. page 5, lines 8 to page 6, line 9. For instance, the materials may be combined in a sandwich-like fashion by layering premeasured quantities onto the skin (see page 6, lines 1-6). Alternatively and further regarding claim 35, the reaction components may be converted into aqueous gels prior to combination and reaction (see page 5, lines 1-4). In this case, the second acid gel behaves as a releasing agent since all reactants are dissolved instead of powdered (see page 5, lines 1-4). Regarding claim 13, when prepared as gels, the gelatin macromolecules are associated through dipole-dipole interaction into elongated or threadlike aggregates; the dispersing medium is held in the interstices among the interlacing network of gelatin macromolecules. In this case dissolution medium is preferably aqueous (see page 5, line 29). As such, the interstices meets the limitation

of a pore as in claim 5, and the water filling these pores meets the limitation of a fluid in claim 5 and the limitation of a low-molecular-weight liquid as in claims 13 and 47. Thus Seitz taught the concept of sequestering reactants in compartments from which the reactants can be released and allowed to react at a controlled rate in order to form NO.

Regarding claims 1, 2, 5, 36, and 39, Seitz did not teach sequestration of the reactants by nanofibers.

Wheatley teaches polymeric, fiber matrix delivery systems for bioactive compounds (see page 3, lines 28-34). The delivery systems are comprised of polymeric fibers having submicron and/or micron diameters (see page 1, lines 7-10) wherein the fibers may be arranged as matrices, linear assemblies, or braided or woven structures (see page 6, lines 9-11). Submicron diameter is defined as approximately 1 to 100 nanometers (see page 5, lines 33-35). Wheatley defines the state of the art related to these nanometer sized polymeric fibers in teaching that they can be made by electrospinning (page 3, lines 1-3), although it is noted that the "electrospinning or gas-jet method" recitation in claim 1 is product-by-process language, which is not granted patentable weight. See MPEP 2113, which states that even though product by process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production, if the product in the product by process claim is the same or obvious from a product of the prior art, the claim is unpatentable even though the prior art was made by a different process. *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985). These fibers provide methods for modulating the rate of release of a bioactive

compound from a delivery system wherein the bioactive compound has been incorporated within or between polymeric fibers (see page 4, lines 7-11). The bioactive agent diffuses, and the time delay can be controlled by varying factors such as polymer diameter and quantity of bioactive agent loaded in the fiber (see page 7, line 29 through page 8, line 2).

Both the Seitz and Wheatley references are directed to combined substrates (i.e., polymeric fibers, layered gels) for the controlled administration of bioactive compounds. Thus, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to utilize the polymer fiber substrates as taught by Wheatley in place of the gel substrates taught by Seitz, with a reasonable expectation of success. One would have been motivated to do so since Wheatley teaches that these polymeric fiber systems allow controlled modulation of the rate of release of bioactive compounds (see page 4, lines 6-16).

Claims 8 and 42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Seitz, *et al.* (WO 01/89572 A1, published November 29, 2001) in view of Wheatley, *et al.* (WO 02/00149 A1, published January 3, 2002) as applied above, and further in view of Santerre et al. (US 5,798,115, patented Aug. 1998).

The teachings of Seitz and Wheatley are delineated above. It is noted that Wheatley teaches that the fibers can be selected from a variety of polymers (see page 6, lines 15-24). Neither of these references teaches the urethane prepolymer and diamine or diol as required in claims 8 and 42.

However, Santerre et al. teach bioresponsive pharmacologically active polymers and articles made therefrom. The invention relates to polymeric compounds and substrates such as implantable medical devices formed from or coated with the pharmacologically active polymeric materials. Pharmacological agents are released in response to in vivo activation at a desired location in a mammal. The pharmacologically active compounds provide in vivo enhanced long term anti-inflammatory, anti-bacterial, anti-microbial, and/or anti-fungal activity (see abstract, in particular). In particular, Santerre et al. teach a diisocyanate (polyurethane prepolymer) reacting with a surface-activated tubing material by reaction of free diisocyanates with active carboxylic acid, amine, or hydroxyl groups (see column 11, lines 25-30). For instance, in Example 4 (see column 16, lines 20-37), hexamethylene diisocyanate is reacted with Jeffamine-900 polyether diamine following addition of the active agent.

Both Wheatley and Santerre are directed to implantable devices for controllably administering bioactive compounds. Thus, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to react the diisocyanate (polyurethane prepolymer) with diamine as taught by Santerre et al. in the polymer devices of Wheatley et al., with a reasonable expectation of success. One would have been motivated to do so since Santerre et al. teach that the pharmacologically active fragment is reacted from a polymeric backbone in *in vivo* applications benefitting from reduced incidence of infection due to the presence of access devices. One further would have been motivated to do so since the *in vivo*

pharmacological activity may be for example, anti-inflammatory in nature (see column 6, lines 16-67).

Claims 9 and 43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Seitz, *et al.* (WO 01/89572 A1, published November 29, 2001) in view of Wheatley, *et al.* (WO 02/00149 A1, published January 3, 2002) as applied above, and further in view of Anand et al. ("Ion-exchange resins: carrying drug delivery forward", DDT Vol. 6, No. 17, September 2001).

The teachings of Seitz and Wheatley are delineated above. Neither of these references teaches that a reactive component is bound to an ion-exchange resin bead as in pending claims 9 and 43.

However, Anand et al. teach that ion exchange resin beads are comprised of a structural component consisting of a polymer matrix and a functional component to which the counter ion is bound (see page 906, end of first column). Specifically, these beads are applicable to drug delivery systems (see page 908, column 1, paragraph 1).

Both Wheatley and Anand are directed to implantation devices for the administration of bioactive agents. Thus, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to utilize the ion exchange resin beads as taught by Anand et al. in the polymers for drug delivery as taught by Wheatley et al., with a reasonable expectation of success. One would have been motivated to do so in order to improve the controlled- or sustained- release of drug dosage, particularly since Anand et al. teach that ion exchange resins impart desirable

flexibility in designing drug delivery systems since these resins release the drug more uniformly than would a simple matrix (see page 908, column 1, paragraph 2).

Claims 12 and 46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Seitz, *et al.* (WO 01/89572 A1, published November 29, 2001) in view of Wheatley, *et al.* (WO 02/00149 A1, published January 3, 2002) as applied above, and further in view of Keefer et al. (US 5,650,447, patented Jul. 1997, submitted in IDS of 1/4/2006).

The teachings of Seitz and Wheatley are delineated above. It is not apparent from these disclosures that one of the fibers necessarily dissolves or swells in the presence of a releasing agent as required by pending claims 12 and 46.

Keefer et al., however, teach the administration of nitric oxide by release from a polymeric material in order to deliver ameliorating, prophylactic, or therapeutic drug dosing for restenosis and related disorders (see abstract, in particular). Specifically, Keefer et al. explicitly teach that the polymer of the polymer-bound compositions may dissolve in a physiological environment in order to desirably deliver the active agent (see column 9, lines 5-7).

Both Seitz and Keefer are directed to devices for the prophylactic or therapeutic administration of nitric oxide. Thus, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to employ the polymer dissolution feature as taught by Keefer et al. in the devices of Seitz, with a reasonable expectation of success. One would have been motivated to do so in order to impart the

biodegradable feature as taught by Keefer et al., thereby eliminating the need for fiber removal post delivery of the bioactive agent.

Response to Arguments

Applicants' arguments presented 12/06/2010 have been fully considered but are unpersuasive. As noted above, all rejections previously presented and not re-iterated herein are withdrawn. Applicants' positions against cited references are summarized and responded to as follows.

Regarding Applicant's argument that the previously cited reference did not teach the reaction of the first and second reactive components to form a reaction product as claimed, this argument is persuasive. For this reason, the instant Office action is non-Final and new grounds of rejection are presented herein.

Applicants argue that the invention of independent claims 1 and 35 is drawn to a fibrous assembly of nanofibers in particular and that the disclosure of the Stamler reference does not teach this limitation. Applicants' argument has been considered but is not persuasive in view of the new grounds of rejection presented above.

Regarding each of secondary references Chu, Trescony, Santerre, Anand, and Keefer, Applicants argue that these references do not teach the alleged deficiency of primary reference Stamler. It is noted that Applicants present no arguments against the relevance of the aforementioned cited secondary references. As such, the relevance of these references is maintained for the reasons of record.

Conclusion

No claims are found allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to AUDREA J. BUCKLEY whose telephone number is (571)270-1336. The examiner can normally be reached on Monday-Thursday 7:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Fereydoun Sajjadi can be reached on (571) 272-3311. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/AJB/

/Richard Schnizer/
Primary Examiner, Art Unit 1635